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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Houghton et al.		
Serial No.:	09/627,694	Examiner:	A. Harris
Filed:	28 July 2000	Art Unit:	1642

For: Method and Compositions for Stimulation of an Immune Response to Differentiation Antigen Induced by Altered Differentiation Antigen

REPLY BRIEF FOR APPELLANT

This paper is filed in response to the Examiner's Answer mailed on May 20, 2003. The Examiner's Answer, like the Office Actions preceding it, is rich in assertions concerning the alleged state of the art, and regrettably lacking in specific citations which might guide the Board and Applicants in testing the merits of these assertions.

Important among the totally unsubstantiated allegations is the assertion on Page 4 of the Answer that "one of ordinary skill in the art would have been motivated to [make human gp75 in insect cells] with a reasonable expectation of success because it is art known that sources of altered antigen can induce immune responses, such as tumor rejection." Substantially the same unsupported allegation was made in the final Office Action, and it was challenged then by Applicants. This allegation was not repeated as motivation in the Advisory Action, because there is no support for it in the art. It is therefore both surprising and inappropriate that it should reappear in the Examiner's Answer, again as a mere conclusory allegation without any support.

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450 on July 11, 2003.

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July 11, 2003

Date of Signature

The discovery that altered antigens are effective for stimulating an immune response, and more importantly for breaking tolerance (i.e., the failure of the immune system to recognize an antigen as foreign) which prevents the development of an effective response against most cancers is the discovery of the present Applicants and is the basis for this application. The Examiner has therefore once again substituted the Applicants' own teaching for the motivation to combine references. This is improper and without this critical element of an obviousness rejection, the rejection cannot stand.

Furthermore, the Examiner has asserted that "Appellants have not provided any unique or unexpected properties." (Examiner's Answer, Page 5). This assertion is incorrect. As noted in the Appeal Brief on Page 6, the entire premise of the Examiner's argument is that a person skilled in the art would expect gp75 made in insect cells to be just like gp75 made in syngeneic cells, and that this protein would be expected to act the same as natural gp75 or syngeneically expressed gp75. At no time has the Examiner argued otherwise. The fact is, however, as clearly established by Example 3 in the specification, mouse gp75 when expressed in insect cells resulted in auto-antibody generation against mouse gp75 in 135 of 138 mice, while no antibodies were detected in any of the 46 controls immunized with syngeneically expressed mouse gp75. This is plainly a result which is both beneficial and not predictable from the mere knowledge that at least some proteins can be cloned in insect cells.

Applicants would point out that the Examiner has, without evidence, elevated the cloning of proteins in insect cells to a "popular technique" (Examiner's Answer, Page 7) apparently to bolster the concept that choosing to express anything and everything in this system is obvious. There is no evidence of record that insect cell cloning is popular, there is only evidence that it is a known technique. The Examiner, also without support, asserts that when using insect cells "inevitably there is high production of recombinant proteins." As reflected in the Appeal Brief, there is nothing inevitable about it, there is not even a clear understanding that all proteins will be

produced, and there is reason in the record (Bouchard) to doubt that a difficult protein like gp75 will be produced and correctly processed.

Finally, the Examiner's position that to prevail Applicants must present evidence "contrary to the facts that the baculovirus expression system lends itself to increased protein propagation of a protein of interest and that said protein would be produced, modified and processed" stands reason and the law on its head. The only proteins that matter in the context of this invention are human differentiation antigens such as gp75. The Examiner has already discounted the statement in the Ausubel reference relied upon that not all proteins are expressed, and art (Bouchard) which would suggest that expression of proteins of this type in even mammalian cells that lack melanocytes could not be predicted . It seems unlikely therefore that a showing relating to any protein other than one within the scope of the claims would convince the Examiner, but this would require the Applicant to prove that the invention which is being claimed does not work. The law does not require such a showing to refute an argument which is crafted from hindsight and which ignores the state of the art and the properties of the products claimed.

For all of these reasons, and those stated in the Appeal Brief, the Examiner has failed to present a sustainable obviousness rejection. Reversal of the rejection is therefore urged.

Respectfully submitted,

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